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10/508,337	04/25/2005	Yoshiaki Kawashima	12480-000063/US	5676

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EXAMINER	
HELM, CARALYNNE E	
ART UNIT	PAPER NUMBER
1615	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/508,337	KAWASHIMA ET AL.	
	Examiner	Art Unit	
	CARALYNNE HELM	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-21,23-30,37-42,45 and 53-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-21,23-30,37,39-42,45,53-63,65 and 66* is/are rejected.

7)☒ Claim(s) *38 and 64* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 September 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election **without** traverse of Group I in the reply filed on January 4, 2008 is acknowledged. The claims drawn to the nonelected invention were cancelled by the applicant. The restriction is deemed proper and thereby made FINAL.

Applicant is advised that should claim15 be found allowable, claim 39 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Objections

Claims 21, 38, and 64 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 21 recites limitations that are broader than its parent in the recitation that the carrier particle is combined with lubricant particles as an alternative to the required dry mechanical particle combining method or fluid bed granulation method. This alternate option is not

recited in the parent claim. Claim 10, from which claim38 ultimately depends, already includes the limitations recited in claim 38. Similarly, claim 59, from which claim 64 depends, already includes the limitations recited in claim 64.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 65-66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 65-66 recite the limitation "the carrier particle" in lines 7-8 of claim 65 and in lines 12-13 of claim 66. There is insufficient antecedent basis for this limitation in the claim. Since no carrier particle is utilized in the method to make the claimed composite (e.g. in a combining step or primary particle preparation step), it is not clear what is done with the recited carrier particle in claims 65 and 66. Therefore these claims cannot be further addressed in regards to prior art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The four factual inquires of Graham v. John Deere Co. have been fully considered and analyzed in the rejections that follow.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 10-11, 14-16 and 38-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jain et al. reference B (previously cited) in view of Schaafsma et al.

(International Journal of Pharmaceutics 2000 193:175-187) and as evidenced by the Sieve Comparison Chart (www.starch.dk/isi/tables/screens.htm 1999).

Jain et al. reference B teaches the preparation of rapidly disintegrating solid oral dosage forms (see abstract). The dosage forms are composed of the active agent in nanoparticle form sized below 1000 nm (see abstract and column 5 lines 58 and 60). The preparation of the final solid dosage form includes the granulation of the nanoparticles along with an aqueous polymer binder via fluidized bed granulation followed by tableting which employs fluidized bed granulation and/or direct compression (see column 11 lines 6-12 and 22-26 and example 3; instant claims 11, 15-16, and 38-39). After the initial granulation process, the product is passed through a standard sized sieve (see example 3). In one example the sieve has a pore size of 430 to 500 mm; since the nanoparticle starting material was 151 nm the granulate must be sized between the pore size of the sieve and the size of a single nanoparticle (see example 3 with #35 sieve and Sieve Comparison Chart; instant claim 14). In the tableting step, the active agent granulate is combined with pharmaceutical excipients. Since the dosage forms are taught to be fast disintegrating, it is clear that they are reduced from the single unit of collected particles to a solubilized or at least separated form. At the point of separation, the particles are no longer collected, therefore the solid dosage from of Jain et al. reference B is considered as a reversible collection. In light, of their teachings of methodologies to generate their taught dosage form, it would have been obvious to one of ordinary skill in the art at the time of the invention to utilize direct compression to combine the granulated nanoparticle and excipient particles into their dosage forms.

Jain et al. reference B do not explicitly describe their fluidized bed granulation process as "dry" or the combination of primary particles made of nanoparticles.

The teachings of the phenomenon involved in fluidized bed granulation provided by Schaafsma et al. where a binder liquid is sprayed onto a fluidized bed of particles and evaporates is the same as that taught by the instant applicants as a fluid bed "dry" granulation process. Thus the fluidized bed granulation process taught by Jain et al. reference B meets the limitations of applicants' claimed fluid bed dry granulation process. In addition, Schaafsma et al. teach the mechanism of granule formation which includes sets of particles that have formed separate larger particles combining together (combining of primary particles – see figure 6C and 10C). Thus the formation and combination of primary particles occurs in fluidized bed granulation in general and specifically in the process taught by Jain et al. reference B (see instant claim 10). Therefore claims 10-11, 14-16 and 38-39 are obvious over Jain et al. reference B and Schaafsma et al. as evidenced by the Sieve Comparison Chart

Claims 10-12 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jain et al. reference B in view of Schaafsma et al. as evidenced by the Sieve Comparison Chart as applied to claims 10-11, 14-16 and 38-39 above, and further in view of Kawashima et al. (previously cited)

Jain et al. reference B in view of Schaafsma et al. as evidenced by Sieve Comparison Table make obvious the limitations of instant claim 10. While Jain et al. reference B teach that many methods can be used to generate the nanoparticles used

in the invention, they do not explicitly teach spherical crystallization (see column 10 lines 14-17).

Kawashima teaches drug nanoparticles as improved drug delivery configurations due to their small size (see page 1 column 1 paragraphs 1 and 2). He goes on to teach several methods for making such particles, including spherical crystallization (see page 1 column 2 paragraph 2; instant claims 12 and 37). Since Dickinson et al. teach that nanoparticles are from 1 nm to 1000 nm in diameter, the nanoparticles of Kawashima are interpreted to be less than 1000 nm (see page 1 lines 10-11).

As a methodology that was known to generate nanoparticles of pharmaceutical actives, it would have been obvious to one of ordinary skill in the art at the time of the invention to use it to generate the nanoparticles of Jain et al. reference B in view of Schaafsma et al. Therefore claims 10-12 and 37 are obvious over Jain et al. reference B in view of Schaafsma et al. and Kawashima et al. as evidenced by the Sieve Comparison Chart.

Claims 10-11, 17-21, and 40-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jain et al. reference B in view of Schaafsma et al. as evidenced by Sieve Comparison Chart as applied to claims 10-11, 14-16 and 38-39 above, and further in view of Carli et al. (US Patent No. 6,355,273).

Jain et al. reference B in view of Schaafsma et al. make obvious the limitations of instant claims 10 and 11. In these teachings they teach the combination of a granulated nanoparticle with an excipient. In one example, the excipient is a cellulose derivative

(Ac-di-sol - a carrier) (see example 1; instant claims 19 and 41). Since the compression of the active granules and excipient particles result in a unitary dosage form where the particles are stuck together, the final structure can be interpreted as including active agent granules adhered to the surface of the excipient particles and vice versa (see instant claims 17 and 40). This modified reference does not explicitly teach the size of the excipient.

Carli et al. teach solid particles that particularly taught for use as tableting excipients beneficial for direct compression (see column 6 lines 21-39). In one embodiment, the particle are composed of the Ac-Di-Sol cellulose derivative and sized at 800 to 1400 μm (see example 3; instant claims 17 and 40). Routine optimization of the particle sizes would have been obvious to one of ordinary skill in the art (note example 7 yields particles 500 to 900 μm; instant claim 18). Further, in this process the particles are extruded then spheronized which results in the smoothing of the surface by a dry mechanical method (see example 1; instant claims 20-21 and 42)

It would have been obvious to one of ordinary skill in the art at the time of the invention to select the cellulose particles of Carli et al. since they are specifically envisioned for tableting via direct compression. Therefore claims 10-11, 17-21, and 40-42 are obvious over Jain et al. reference B in view of Schaafsma et al. and Carli et al. as evidenced by Sieve Comparison Chart.

Claims 10 and 53-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jain et al. reference B in view of Schaafsma et al. as evidenced by Sieve

Comparison Chart as applied to claims 10-11, 14-16 and 38-39 above, and further in view of Hosokawa et al. (previously cited)

Jain et al. reference B in view of Schaafsma et al. make obvious the limitations of instant claim 10. In addition, to direct compression, Jain et al. reference B teach dry granulation as a means of tableting in the nanoparticle containing granulate. This modified reference does not explicitly teach the machinery of instant claim 53.

Hosokawa et al. teach an apparatus as well as its method of use for granulating (agglomerating) powdered materials (see abstract). In particular, the device allows for the combination of powdered materials via dry mechanical impact (see column 1 lines 6-18). The device is taught to have a cylindrical rotator with a receiving face that faces the center and press head all housed within a casing and sharing the same vertical axis (see column 4 lines 19-24 and 33-38; instant claim 53). The press heads press the material to be treated to the receiving face of the casing to combine particles with one another (see column 4 lines 33-45; instant claim 53). The press heads themselves are depicted as semicircular with a curvature greater than that of the receiving face (see figures 6 and 14; instant claims 54-55).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use dry granulation instead of direct compression in the tableting step taught by Jain et al. reference B as a one of a finite set of equivalent methods taught to reach the same end. The apparatus of Hosokawa et al. was known at the time of the invention as a means by which to perform dry granulation to combine particles, thus it would have been obvious to one of ordinary skill in the art to use this apparatus as

intended in the tableting step of Jain et al. reference B in view of Schaafsma et al. as evidenced by the Sieve Comparison Chart. Therefore claims 10 and 53-55 are obvious over Jain et al. reference B in view of Schaafsma et al. and Hosokawa et al. as evidenced by the Sieve Comparison Chart.

Claims 59, 61, and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jain et al. reference B in view of Schaafsma et al.

Jain et al. reference B teach the preparation of rapidly disintegrating solid oral dosage forms (see abstract). The dosage forms are composed of the active agent in nanoparticle form sized below 1000 nm (see abstract and column 5 lines 58 and 60). The preparation of the final solid dosage form includes the granulation of the nanoparticles in via fluidized bed granulation followed by tableting which employs fluidized bed granulation and/or direct compression (see column 11 lines 6-12 and 22-26). In the tableting step, the active agent granulate is combined with pharmaceutical excipients. In one example, the excipient is a cellulose derivative, a known particulate excipient (see example 1). Since the compression of the active granules and excipient particles result in a unitary dosage form where the particles are stuck together, the final structure can be interpreted as including active agent granules adhered to the surface of the excipient particles and vice versa (see instant claim 61). Additionally, since the dosage forms are taught to be fast disintegrating, it is clear that they are reduced from the single unit of collected particles to a solubilized or at least separated form. At the point of separation, the particles are no longer collected, therefore the solid dosage from

of Jain et al. reference B is considered as a reversible collection. In light, of their teachings of methodologies to generate their taught dosage form, it would have been obvious to one of ordinary skill in the art at the time of the invention to utilize a fluidized bed granulation process to combine the granulated nanoparticle and excipient particles into their dosage forms. Jain et al. reference B do not explicitly describe their fluidized bed granulation process as "dry". However, the teachings of the phenomenon involved in fluidized bed granulation provided by Schaafsma et al. where a binder liquid is sprayed onto a fluidized bed of particles and evaporates is the same as that taught by the instant applicants as a fluid bed "dry" granulation process. Thus the fluidized bed granulation process taught by Jain et al. reference B meets the limitations of applicants claimed fluid bed dry granulation process. Therefore claims 59, 61, and 64 are obvious over Jain et al. reference B in view of Schaafsma et al.

Claims 59-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jain et al. reference B in view of Schaafsma et al. as applied to claim 59 above, and further in view of Carli et al..

Jain et al. reference B in view of Schaafsma et al. make obvious the limitations of claim 59. This modified reference does not explicitly teach the size of the excipient.

Carli et al. teach solid particles that particularly for use as tableting excipients that are beneficial for direct compression (see column 6 lines 21-39). In one embodiment, the particles are composed of the Ac-Di-Sol cellulose derivative and sized at 800 to 1400 μm (see example 3; instant claims 17 and 40).

It would have been obvious to one of ordinary skill in the art at the time of the invention to select the cellulose particles of Carli et al. since they are specifically envisioned for tableting. Therefore claims 59-60 are obvious over Jain et al. reference B in view of Schaafsma et al. and Carli et al.

Claim 62 is rejected under 35 U.S.C. 103(a) as being unpatentable over Staniforth et al. (US PGPub No. 2003/0175214) in view of Trofast et al. (previously cited).

Staniforth et al. teach a composition for inhalation composed of carrier particles to which are attached an additive to promote the release of the drug particles that are also attached to the carrier (see abstract, paragraphs 2, 7, and 10). The additive is taught as a biocompatible glidant (lubricant) where starch (polymer) is envisioned (see paragraphs 40 and 50). In addition, the additive is envisioned at 100 nm in diameter (see paragraph 57).The active (drug) particles are from 0.01 up to 15 μm in size, while the carrier is at least 50 μm (see paragraphs 11 and 69). Further, Staniforth teach the modification of the carrier surfaces with the glidant/lubricant before adherence of the drug particles to the carrier surface (see example 1). This reference does not explicitly teach the formation of primary particles from drug nanoparticles.

Trofast et al. teach a method of agglomerating fine drug particles via a dry process such that the agglomerated particles (composite particles) would be able to break up into their substituent particles during inhalation (page 2 lines 10-21, page 4 lines 7-8, page 5 lines 6-9). In addition, they teach that finely divided particles (those

less than 10 μm in diameter) are difficult to handle and meter, but their agglomeration method alleviates these issues (see page 1 lines 15-21).

It would have been obvious to one of ordinary skill in the art at the time of the invention to select the biocompatible polymer, starch, as the glidant in the invention of Staniforth et al. based on their explicit teachings of this particular compound. In addition, since Trofast et al. teach 1) the difficulty in handling particles less than 10 μm, 2) a method of agglomerating such particles to alleviate this issue, and 3) particularly envision their method of collection of particles for solid inhalation compositions, it would have been obvious to one of ordinary skill in the art to apply their method to the drug the particles of Staniforth et al. (e.g. those 0.01 to 10 μm) such that the agglomerates are below 15 μm as taught, and easier to handle during processing. The result of this reference combination would be the agglomerated (primary) drug particles being used as the active particles of Staniforth et al. such that 1) carrier particles larger than the primary/drug particles would be modified with a nanoparticulate biocompatible polymer ("nano" particle size taught by Staniforth et al.) followed by 2) the combination of the primary/drug particles with one another by adherence to the modified carrier particles. Therefore claim 62 is obvious over Staniforth et al. in view of Trofast et al.

Claims 23-27, 30, and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ishizaka et al.(previously cited) in view of Jain et al. reference B, and Ryde et al. (previously cited)

Ishizaka et al. teach a dry method of making a composite particle with a drug containing parent or core particle (described as product A by reference), which ranges in size from 0.5μm to 1mm, and smaller child biocompatible polymer particles that are fixed to the surface (see column 3 lines 57-58, column 4 lines 40-47, and column 6 lines 3-5 and 12-13, column 7 lines 8-15; instant claim 23). Polyethylene glycol, starch, and hydroxypropyl cellulose are taught as envisioned polymers within the invention (see column 3 lines 46-53). This reference does not explicitly teach that the polymer is a lubricant.

Ryde et al. teach the production of a composite pharmaceutical where a surface stabilizer is adsorbed to the surface of a drug and both are sized such that the composite is less than about 1μm in size (e.g. both the drug and surface stabilizer are less than 1μm in size) (see column 6 lines 24-33 and column 7 lines 32-34; instant claims 23, 24, 30, and 45). Mechanical means are taught for adhering the stabilizer to the particle surface (see column 9 lines 34-35). A variety of materials are taught by Ryde et al. as surface stabilizers including hydroxypropyl cellulose and starch (see column 7 lines 40-43).

Jain et al. reference B teaches the production of a nanoscale composite pharmaceutical where a surface modifier (lubricant) is adsorbed to the surface of a drug (see column 5 lines 44-64 and column 6 lines 29-32; instant claims 23 and 24). These surface materials include polyethylene glycol, glycerol monostearate (sugar ester), colloidal silicon dioxide (colloidal silica), and hydroxypropylmethyl cellulose phthalate (see column 7 lines 34, 37, 45, and 49-50; instant claims 24-27 and 30).

Since Ishizaka et al., Ryde et al, and Jain et al. reference B each teach functional equivalents for polymeric materials that are adsorbed to drug particles as surface modifiers, it would have been obvious to one of ordinary skill in the art to exchange the polyethylene glycol taught to by Ishizaka et al. for glycerol monostearate (sugar ester) or colloidal silicon dioxide. Both Ryde et al. and Ishizaka et al. teach mechanical means for adhering the surface stabilizer polymer to the drug particle surface indicating that such a methodology was known at the time of the invention. Further, the teachings of Ishizaka et al. about the sizing of their composite particles, core particles and child particles would have equipped and made it obvious to one of ordinary skill in the art to size the drug particles at 500 μm and the polymer above or below 1000 nm. Therefore claims 23-27, 30, and 45 are obvious over Ishizaka et al. in view of Jain et al. reference B and Ryde et al.

Claims 23-24 and 28-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ishizaka et al. in view of Jain et al. reference B and Ryde et al. as applied to claims 23-27, 30, and 45 above, and further in view of Kawashima and Murakami et al. (previously cited).

Ishizaka et al. in view of Jain et al. reference B and Ryde et al. make obvious the claimed method of preparing composites of drug particles coated by biocompatible polymer particles where the polymer is also known as a pharmaceutical excipient. The modified reference does not explicitly teach nanoparticulate PLGA produced by spherical crystallization as the biocompatible polymer.

Kawashima teaches the production of poly(lactic acid-co-glycolic acid) copolymer (PLGA) containing nanoparticles by spherical crystallization (see page 1 column 2 paragraph 1).

Murakami et al. teach that PLGA nanoparticles were well known as pharmaceutical excipients (see page 213 paragraph 1). One of ordinary skill would have found it obvious to apply this known component as a surface modifier in the invention of Ishizaka et al. in view of Jain et al. reference B and Ryde et al. with a reasonable expectation of success. Since Kawashima teaches PLGA nanoparticles made by spherical crystallization, it also would have been obvious to employ this method as one of a finite number of options known at the time of the invention. Therefore claims 23-24 and 28-29 are obvious over Ishizaka et al. in view of Jain et al. reference B, Ryde et al., Kawashima, and Murakami et al.

Claims 23 and 56-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ishizaka et al. in view of Jain et al. reference B and Ryde et al. as applied to claims 23-27, 30, and 45 above, and further in view of Hosokawa et al.

Ishizaka et al. in view of Jain et al. reference B and Ryde et al. make obvious the claimed method of preparing composites of drug particles coated by biocompatible polymer particles. This modified reference does not explicitly teach the use of the machinery of claim 56

Hosokawa et al. teach an apparatus as well as its method of use for granulating (agglomerating) powdered materials (see abstract). In particular, the device allows for

the combination of powdered materials via mechanical impact (see column 1 lines 6-18). The device is taught to have a cylindrical rotator with a receiving face and press head all housed within a casing (see column 4 lines 19-24 and 33-38; instant claim 56). The press heads press the material to be treated to the receiving face of the casing to combine particles with one another (see column 4 lines 33-45; instant claim 56). The press heads themselves are depicted as semicircular with a curvature greater than that of the receiving face (see figures 6 and 14; instant claims 57-58). Hosokawa et al. go on to teach the apparatus for the coating of particles with other more fine particles where particles can range from 0.001-5 microns and 1-50 microns (see column 12 line 63-column 13 line 6).

The apparatus of Hosokawa et al. was known at the time of the invention as a means by which to mechanically combine particles into composite particles such that fine particles coated larger particles and had starting materials that were in the size range envisioned by Ishizaka et al. in view of Ishizaka et al. in view of Jain et al. reference B and Ryde et al. Thus it would have been obvious to one of ordinary skill in the art at the time of the invention to use the apparatus of Hosokawa et al. to produce the mechanically combined composite particles of Ishizaka et al. in view of Trofast et al. and Jain et al. reference B as a known option within their technical grasp. Therefore claims 23 and 53-56 are obvious over Ishizaka et al. in view of Jain et al. reference B, Ryde et al., and Hosokawa et al.

Response to Arguments

Applicants' arguments, filed July 10, 2008 and August 8, 2008, have been fully considered but they are not deemed to be persuasive regarding the rejection of claims 23-30 and 45.

The double patenting and provisional double patenting rejections are moot in light of the amendments to the claims therefore they are hereby withdrawn.

Regarding rejection s over Ishizaka et al. in view of Ryde et al. and Jain et al. reference B under 35 U.S.C. 103(a):

Although Ryde et al. may not explicitly teach that their method modifies the surface of the drug particle by milling the particle with excipients that are adhered to its surface, they perform surface modification. Since milling is a dry mechanical method, it meets the limitation of the instantly claimed dry mechanical method. So contrary to applicant's argument, this collection of references does teach the surface modification of the drug particles by a dry mechanical combining process.

Applicants reiterate these arguments when this set of references is further combined with Hosokawa et al. or Kawashima et al. and Murakami et al. and are similarly disputed as described in the preceding paragraph.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or

newly applied. They constitute the complete set presently being applied to the instant application.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Friday 9-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Caralynne Helm/
Examiner, Art Unit 1615

/Robert A. Wax/
Supervisory Patent Examiner, Art Unit 1615